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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,915	05/04/2001	Jennifer L. Hillman	PF-0247-2 CON	7120

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EXAMINER

HUFF, SHEELA JITENDRA

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 04/07/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/848,915

Applicant(s)

HILLMAN ET AL.

Examiner

Sheela J Huff

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6,8-16,18 and 44-46 is/are pending in the application.
- 4a) Of the above claim(s) 3-6,8-14,18 and 44-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,15 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed on 2/3/03 have been considered. Applicant's arguments are deemed to be persuasive-in-part.

Claims 1-6, 8-16, 18 and 44-46 are pending.

Claims 3-6, 8-14, 18 and 44-46 are withdrawn from consideration.

Claims 1-2 and 15-16 are currently under consideration.

The rejection of claims 17 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the cancellation of claim 17.

The rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of applicant's amendments.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 1 and 15 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The reasons for this rejection are of record in paper no. 7, mailed 10/29/02.

Applicant argues that the genus is not highly diverse. In support of this, applicant cites Brenner et al. Brenner et al. merely point out (page 6076, 2nd column, 2nd paragraph) that a 30% identity was a reliable threshold for plotting the percent identity of unrelated proteins in a particular database- the PDB90D-B database (Protein Data Bank

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comprising domains with were all less than 90% identical) which contains over 2000 protein domains- (page 6074, 2nd column, 2nd paragraph, and Figure 3). In contrast, applicant is comparing the sequence identity of an unknown protein to the sequence of BUP. Thus, from a statistical view, one of ordinary skill would conclude that applicant does not have the quantity of data to extrapolate the results of Brenner et al.

Furthermore, Brenner et al. teach that high percent identity does not necessarily identify related proteins (Figure 2) wherein the principal reasons percentage identity does so poorly seem to be that it ignores information about gaps and about the conservative or radical nature of residue substitutions (page 6076, 2nd column, 1st paragraph).

Applicant argues that the chemical structure definition of a genus is sufficient and that a functional limitation is not need. Applicant further states that they have defined a chemical structure for SEQ ID No. 1. This is not disputed. Applicant has not defined chemical structures for variants or fragments of SEQ ID No. 1 and this is what the rejection is directed to. In fact, it is applicant that ties in "what amino acids can be varied" to function (see page 5, lines 13-15 of the specification). Determining which amino acids may be changes in dependent on not abolishing the biological or immunological activity. Thus, since the is no known function for the polypeptides, one skilled in the art could not determine which amino acids could be changed without abolishing the function.

Claim Rejections - 35 USC § 101

Claims 1-2 and 15-16 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and a substantial asserted utility or a well established utility. The reasons for this rejection are of record in paper no. 7, mailed 10/29/02.

Applicant argues that use of the claimed polypeptides for diagnosis of conditions or diseases characterized by expression of ^{ICAD} RBTN^H for toxicology testing, and for drug discovery are sufficient utilities under 35 USC 101 and 112, first paragraph and that there is a "well-established" use for the claimed invention, specific practical and beneficial uses for the invention, and that those uses are substantial. Applicants further argue that toxicology testing is a well-established utility. This argument has been considered but is not found persuasive. First, it is noted that toxicology testing is not specifically recited in the specification as originally filed. Further, for a utility to be "well-established" it must be specific, substantial and credible, and the particulars of toxicology testing with regards to SEQ ID NO:1 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO:1. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the

polynucleotide(s) and claimed polypeptides in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicant's individual polynucleotide and encoded polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptides has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any information regarding this polypeptide could be put.

Applicant argues that similarity of the claimed polypeptide to BUP. These arguments have been addressed above.

Applicant further argues that the use of SEQ ID No. 1 for toxicology testing, drug discovery, and disease diagnosis are practical uses that confer "specific benefits" to the public (page 18). Specifically, applicants contend that the rejection is based on a scientifically incorrect and legally unsupportable assertion that identification of the family or families of proteins to which the claimed invention belongs does not satisfy the utility requirement. The rejection is based on the failure to disclose sufficient properties of the protein and/or polynucleotide to support an inference of utility. Moreover, applicant's contend that practical, beneficial use, not functionality, is at the core of the utility

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requirement wherein so long as the practical benefits are apparent from the invention without speculation, the requirement is satisfied. This argument has been considered but is not found persuasive because the practical benefits of SEQ ID No. 1 are, in fact, not apparent nor disclosed. They are merely speculative in that the discovery of polynucleotides encoding SEQ ID No. 1-like proteins is limited to further investigation. And to re-state applicant, "To state that a biological molecule might be useful to treat some unspecified disease is not, therefore a specific utility. *In re Kirk*, 376 F.2d 936, 945, 153 USPQ 48 (C.C.P.A. 1967).

Beginning at page 12, applicants discuss a declaration by Dr. Furness. The declaration under 37 CFR 1.132 filed 2/3/03 (the Furness declaration) is insufficient to overcome the rejection of claims under 35 U.S.C. § 101 and 112, first paragraph as set forth in the last Office action. At paragraph 6, Dr. Furness asserts that the person of ordinary skill in the art would have considered the priority application to have disclosed the use of SEQ ID NO: 1 "as a research tool in a number of gene and protein expression monitoring applications that were well-known at that time to be useful in connection with the development of drugs and the monitoring of the activity of such drugs." At paragraph 8, Dr. Furness states that his consideration of utility focuses on the use of the protein of SEQ ID NO: 1 in gene and protein expression monitoring applications. At paragraph 10, Declarant discusses the prior art with respect to using 2-D PAGE mapping to study regulation of protein expression by drugs and toxic agents.

At page 21, the specification teaches that "A variety of protocols for detecting and measuring the expression of HTAP, using either polyclonal or monoclonal antibodies specific for the protein are known in the art." At page 33-38, the use of the protein (or antibodies thereto) for diagnostic or drug screening techniques is discussed. There is no disclosure of the use of the protein in the type of drug development and toxicology testing urged by Dr. Furness. Utility must be in the form of a specific and substantial *disclosed* utility, or a well-known utility. Further, well-known utility must be specific and substantial. Examples of well-known utilities of protein include, for example the use of insulin in treatment of diabetes. The use of the claimed protein for 2-D PAGE in toxicology testing or drug development does not meet the requirements of 35 U.S.C. § 101 because (a) the use is not well-known, that is, is not of the level of well-known use such as the use of insulin (b) cannot be asserted for *any* protein, and was not asserted for the protein of SEQ ID NO: 1, and (c) does not require the isolation of the protein of SEQ ID NO: 1. Assuming, *in arguendo*, that the drug discovery and toxicology testing discussed in the declaration are "well-known utilities", they would still not satisfy the requirements of 35 USC 101 and 112, first paragraph, since well-known utilities must

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also be specific and substantial. Since the type of testing discussed by Dr. Furness can be done with any new, uncharacterized protein, the asserted utility is not specific. Also, since the specification does not disclose a correlation between any disease state and an alteration in level or form of protein of SEQ ID NO: 1, significant further experimentation would be required of the skilled artisan to establish such a correlation. Thus, these utilities are also not substantial." Further, the uses urged by declarant do not require isolated protein of SEQ ID NO: 1: In the type of analyses urged by Declarant, the proteins themselves are not isolated, nor are antibodies to specific proteins made. Rather, cells are exposed to agents, then cell extracts made, and analyzed to see which "spots" are found on the gel. The methods do not use isolated proteins. Thus, unlike nucleic acid microchips, wherein specific nucleic acid probes must be isolated and affixed to the microchip used in the analysis, the type of analysis argued by Declarant does not require isolated proteins such as that claimed.

At paragraph 12, Declarant argues that given the disclosure that expression of the protein of SEQ ID NO: 1 is associated with uterine tissues, that it would have led the person of ordinary skill in the art working on developing new drugs for the treatment of cell proliferation disorders, and to conclude that a 2-D PAGE map containing the protein of SEQ ID NO: 1 would be more useful than one without. This argument has been fully considered but is not deemed persuasive because as stated above, the PAGE maps are not made using purified samples of individual proteins, but rather are a representation of the total protein content of the cell. Further, since the specification does not establish that the protein of SEQ ID NO: 1 is expressed in any eating disorder in any way that is different from the way it is expressed in normal individuals. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify diseases states which correlate with altered levels or forms of the claimed protein. Therefore, this asserted utility is also not substantial.

MCAD
NHT
YCA
NHT
Finally, Declarant asserts that one would use ELISA, RIA or FACS for measuring NHT, and thus that the protein has utility. This argument has been fully considered but is not deemed persuasive because such analysis, in the absence of any known role of NHT, is considered to be further research on NHT itself, to determine the role, function and properties of the protein. Such use for further research does not meet the requirement of 35 U.S.C. § 101.

As an aside, it is noted that Dr. Furness is a consultant for Incyte Pharmaceuticals, Inc., the assignee in this application, and thus is a concerned party. Further, it is noted that no new facts or evidence on the role, function or properties of the claimed protein have been presented, thus the declaration appears to be largely one of opinion. The declaration has been considered with regard to the discussion of the state of the art, and what is actually disclosed. However, any legal conclusions therein are not entitled to any weight. See *In re Chilowsky*, 306 F.2d 908, 134 USPQ 515 (CCPA 1962) (expert opinion that an application meets the requirements of 35 U.S.C. 112 is not entitled to any weight; however, facts supporting a basis for deciding that the specification complies with 35 U.S.C. 112 are entitled to some weight); and *In re Lindell*, 385 F.2d 453, 155 USPQ 521 (CCPA 1967), and MPEP 716.01(c).

Applicant's further assert (page 25) that the use of the claimed invention for toxicology testing, drug discovery, and disease diagnosis supports a substantial utility wherein the claimed invention's use as a *tool* (i.e. for toxicology testing) is just such a practical, "real-world" use. Applicant asserts that there is no authority for the proposition that use as a tool for research is not a substantial utility. However, as set forth in *In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) and quoting the Board of Patent Appeals, "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates." Thus, Applicant's arguments have not been found persuasive.

Applicant also argues (page 20) that there exists a market "for databases containing all expressed genes". However, this assertion fails to address the utility of the *individually* claimed polypeptides of the invention of the instant application. The claims are to isolated chemical compositions, not to descriptive information included in a database.

Applicants further argue (page 27) that by requiring the patent application to assert a particular or unique utility, the patent examination utility guidelines and training

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materials applied by the Examiner misstate the law. Applicant's argue that such "unique" or "particular" utilities have never been required by law. This argument has been considered but is not found persuasive. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where *specific* benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . . [i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that

would support a conclusion that the HTAP protein of the instant application was, as of the filing date, useful for diagnosis, prevention and treatment of diseases related to dysregulated cell growth and proliferation, including cancer as stated at page 1 of the specification. Until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO: 1, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

Thus, Applicant's arguments have not been found persuasive and the rejection is maintained.

Claims 1-2 and 15-16 remain rejected under 35 U.S.C. 112, first paragraph. The reasons for this rejection are of record in paper no. 7, mailed 10/29/02.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 703-305-7866. The examiner can normally be reached on T,Th 6am-12pm and alternate Mondays 6am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Sheela J Huff
Primary Examiner
Art Unit 1642

sjh
April 3, 2003